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Patent

PRETREATMENT METHOD FOR ENHANCING TISSUE ADHESION

Related Applications

This application is a divisional of co-pending Application Serial No. 09/548,145, filed April 13, 2000, which is continuation-in-part of Application Serial No. 09/140,017, now U.S. Patent No. 6,475,182, and which is a divisional application of Application Serial No. 09/021,708, filed February 10, 1998, now U.S. Patent No. 6,302,898, which is a continuation-in-part of Application Serial No. 08/963,033, filed November 3, 1997, entitled "Vascular Sealing Device," now abandoned, Application Serial No. 08/963,082, filed November 3, 1997, entitled "In Situ Formed Non-fluent Closure Composition," now abandoned, and Application Serial No. 08/963,408, filed November 3, 1997, now U.S. Patent No. 6,033,401, which each claim the benefit of Provisional U.S. Application Serial No. 60/036,299, filed March 12, 1997.

Field of the Invention

This invention relates to a vessel closure device, and more particularly to a device for effecting the closure of a vessel by delivering a fluent closure composition precursor and converting the composition in situ to a non-fluent closure composition.

Background of the Invention

A wide variety of surgical procedures are

performed by the introduction of a catheter into a vessel. After the surgical procedure is completed, closure of the vessel at the site where the catheter was introduced is needed. Vessel punctures formed in the process of performing a catheter based surgical procedure are commonly 1.5 mm to 7.0 mm in diameter and can be larger. Closure of these punctures is frequently complicated by anticoagulation medicine given to the patient that interferes with the body's natural clotting abilities.

Closure of a vessel puncture has traditionally been performed by applying pressure to the vessel adjacent the puncture site. This procedure requires the continuous attention of at least one medical staff member to apply pressure to the vessel puncture site and can take as long as 30 minutes.

Devices have been developed for effecting the closure of vessel punctures through the application of energy. See U.S. Patent Nos. 5,626,601; 5,507,744; 5,415,657; and 5,002,051. Devices have also been developed for effecting the closure of vessel punctures through the delivery of a mechanical mechanism which mechanically seals the puncture. See U.S. Patent Nos.: 5,441,520; 5,441,517; 5,306,254; 5,282,827; and 5,222,974. Devices have also been developed for effecting the closure of vessel punctures through the delivery of a composition to block the vessel puncture. See U.S. Patent Nos. 5,601,602; 5,591,205; 5,441,517; 5,292,332; 5,275,616; 5,192,300; and 5,156,613. Despite the various devices that have been developed for closing vessel punctures, a need still exists for a simple, safe and inexpensive device and method for closing vessel punctures.

Summary of the Invention

The present invention relates to a device and

method for sealing a puncture in a body vessel. In one embodiment, the device has an elongated body having a proximal end and a distal end sized to be positioned within a lumen of the body vessel; at least one closure composition precursor lumen within the elongated body having a entrance port adjacent the proximal end of the elongated body through which one or more fluent closure composition precursors can be delivered into the closure composition precursor lumen and an exit port adjacent the distal end of the elongated body through which the one or more fluent closure composition precursors can be delivered outside the vessel adjacent the vessel puncture; and at least one position sensing mechanism positioned distal relative to the exit port such that the exit port is outside the vessel when the at least one position sensing mechanism is detected to be outside the vessel.

The closure device of this embodiment may optionally further include an energy delivery device for delivering energy adjacent the distal end of the elongated body to the fluent closure compound precursor.

In one variation, the device includes a microwave antenna for delivering microwave energy adjacent the distal end of the elongated body to the fluent closure compound precursor. In another variation, the device includes a waveguide for delivering light energy adjacent the distal end of the elongated body to the fluent closure compound precursor. In yet another variation, the device includes a RF electrode for delivering RF energy adjacent the distal end of the elongated body to the fluent closure compound precursor.

In another embodiment, the device includes an elongated body having a proximal end and a distal end sized to be positioned within a lumen of the body vessel; at least one closure composition precursor lumen within

the elongated body having a entrance port adjacent the proximal end of the elongated body through which one or more fluent closure composition precursors can be delivered into the closure composition precursor lumen and an exit port adjacent the distal end of the elongated body through which the one or more fluent closure composition precursors can be delivered outside the vessel adjacent the vessel puncture; and a microwave antenna for delivering microwave energy adjacent the distal end of the elongated body to the fluent closure compound precursor. The microwave antenna according to this embodiment is preferably incorporated onto the elongated body adjacent the body distal end.

In another embodiment, the device includes an elongated body having a proximal end and a distal end sized to be positioned within a lumen of the body vessel; at least one closure composition precursor lumen within the elongated body having a entrance port adjacent the proximal end of the elongated body through which one or more fluent closure composition precursors can be delivered into the closure composition precursor lumen and an exit port adjacent the distal end of the elongated body through which the one or more fluent closure composition precursors can be delivered outside the vessel adjacent the vessel puncture; a guidewire lumen within the elongated body; and a guidewire including microwave antenna for delivering microwave energy adjacent the distal end of the elongated body to the fluent closure compound precursor.

The present invention also relates to a method for sealing a puncture in a body vessel. In one embodiment, the method includes the steps of delivering a distal end of an elongated body into a lumen of the body vessel, the elongated body having at least one closure composition precursor lumen with a entrance port adjacent

the proximal end of the elongated body through which one or more fluent closure composition precursors can be delivered into the closure composition precursor lumen and an exit port adjacent the distal end of the elongated body through which the one or more fluent closure composition precursors can be delivered outside the vessel adjacent the vessel puncture, and at least one position sensing mechanism positioned distal relative to the exit port such that the exit port is outside the vessel when the at least one position sensing mechanism is detected to be outside the vessel; withdrawing the elongated body until the at least one position sensing mechanism is positioned outside the vessel lumen; delivering one or more fluent closure composition precursors outside the vessel adjacent the vessel puncture; and transforming the one or more fluent closure composition precursors into a non-fluent closure composition which seals the vessel puncture.

In one variation, the method further includes the step of delivering energy adjacent the distal end of the elongated body to the fluent closure compound precursor to transform the one or more fluent closure composition precursors into the non-fluent closure composition. The energy may be microwave energy and the at least one of the one or more fluent closure composition precursors may optionally include a microwave energy absorbing material.

The present invention also relates to a non-fluent closure composition for closing a puncture in a vessel. In one embodiment, the non-fluent closure composition is formed by delivering a fluent closure composition precursor to a position outside the vessel adjacent to the puncture; and transforming the fluent closure composition precursor *in situ* to a non-fluent closure composition. In another embodiment, the non-

fluent closure composition is formed by delivering two or more fluent closure composition precursors to a position outside the vessel adjacent to the puncture; and mixing the two or more fluent closure composition precursors to
5 form a non-fluent closure composition *in situ* adjacent the vessel puncture.

Transforming the fluent closure composition precursor *in situ* may include solidifying the closure composition precursor or causing the closure composition
10 precursor to chemically react with itself to form a non-fluent composition, the chemical reaction optionally being catalyzed by a catalyst or by energy. Energy used in the method may be any form of energy including, for example, RF energy and microwave energy. When microwave
15 energy is used, the closure composition precursor includes a microwave energy absorbing material.

The present invention also relates to a method for improving the adhesiveness of tissue surfaces to sealants and adhesives by applying energy to a surface of
20 tissue to which a sealant or adhesive is to be applied. The energy thermally modifies the tissue surface and causes the tissue to be more adherent to sealants and adhesives, such as closure composition used in the present invention. The thermal modification preferably
25 includes blanching the tissue surface. The thermal modification is believed to reduce the water content at the tissue surface, remove materials at the tissue surface which interfere with the adhesiveness of tissue surfaces to sealants and adhesives, change the topography
30 at the tissue surface, and preferably increase the surface area at the tissue surface, all of which serve to increase the tissue surface's ability to adhere sealants and adhesives. Thermal modification of the tissue surface may be performed with any suitable form of
35 energy, including for example, electromagnetic energy (RF

energy, light, and microwave energy), ultrasound, and other thermal heat sources.

The present invention also relates to a method for improving the adhesiveness of tissue surfaces to sealants and adhesives by applying a chemical agent to a surface of tissue to which a sealant or adhesive is to be applied. The chemical agent modifies the tissue surface such that the tissue surface is more adherent to sealants and adhesives, such as closure composition used in the present invention. The chemical modification preferably includes denaturing the tissue surface.

In one variation, basic chemical agents (i.e., having a pH greater than 7) capable of modifying a tissue surface are used. Examples suitable basic chemical agents include but are not limited to aqueous sodium bicarbonate, aqueous sodium carbonate, water solutions or suspensions of alkali or alkali earth oxides and hydroxides, aqueous ammonia, water soluble amines such as alkanol amines, basic amino acids such as lysine and poly(lysine), aqueous sodium lysinate, and basic proteins such as albumin.

In another variation, acidic chemical agents (i.e., having a pH less than 7) having an osmolality above that of blood are used which are capable of modifying a tissue surface.

In yet another variation, a chemical agent which can serve as a tissue etchant is used. Examples of suitable tissue etchants include, but are not limited to salicylic acid, carboxylic acids, α -hydroxy carboxylic acids, and peroxides.

Brief Description of the Drawings

Figure 1A is a sideview of a closure device according to the present invention.

Figure 1B is a cut-away view of the closure device of Figure 1 A.

Figure 2 is a cut-away view of a closure device with a first and second closure lumen coupled to first and second closure composition precursor sources.

Figure 3A is a sideview of a closure device including a guidewire lumen configured to accommodate a guidewire.

Figure 3B is a cut-away view of the closure device illustrated in Figure 3A.

Figure 4A illustrates a sheath with a distal end disposed within a vessel.

Figure 4B illustrates a closure device disposed within the sheath such that the distal end of the closure device extends beyond the distal end of the sheath.

Figure 4C illustrates the sheath and closure device withdrawn from the vessel until the position sensing mechanism is located outside the vessel adjacent the puncture.

Figure 4D illustrates a closure composition precursor source coupled to the closure device of Figure 4C. The closure composition precursor is delivered through the closure lumen to the puncture.

Figure 4E illustrates the puncture after the closure device of Figure 4D is withdrawn from the puncture.

Figure 4F illustrates the puncture after the closure device is completely withdrawn from the tissue site.

Figure 5A is a sideview of a locking mechanism coupled to a closure device and threads on a sheath.

Figure 5B is a sideview of the locking mechanism of Figure 5A coupled to the threads on a sheath.

Figure 6A illustrates a sheath with a distal end disposed within a vessel.

Figure 6B illustrates a guidewire disposed within the sheath of Figure 6A.

Figure 6C illustrates the sheath of Figure 6B withdrawn along the guidewire.

5 Figure 6D illustrates a closure device threaded along the guidewire of Figure 6C until the distal end of the device is disposed within a vessel.

10 Figure 6E illustrates the closure device of Figure 6D after the guidewire has been withdrawn. The closure device is withdrawn until the position sensing mechanism is located outside the vessel adjacent the puncture.

15 Figure 6F illustrates a closure composition precursor source coupled to the closure device of Figure 6E. The closure composition precursor is delivered through the closure lumen to the puncture.

Figure 6G illustrates the puncture after the closure device is completely withdrawn from the tissue site.

20 Figure 7A is a sideview of a closure device including a fiber optic ring as an energy delivery device.

Figure 7B is a cross section of the fiber optic ring of Figure 7A.

25 Figure 8A is a sideview of a closure device with a contact switch as a position sensing mechanism.

Figure 8B is a sideview of a contact switch of Figure 8A being compressed by the vessel wall.

30 Figure 9A illustrates a closure device with a plurality of pressure ports coupled to a single position lumen.

Figure 9B illustrates a closure device with a plurality of pressure ports coupled to the same tubing before the tubing is coupled to the pressure sensor.

35 Figure 9C illustrates a closure device with a

plurality of pressure ports and first and second closure lumens.

Figure 10A is a sideview of a closure device including a balloon as the position sensing device.

5 Figure 10B illustrates the closure device of Figure 10A disposed within a vessel.

Figure 11 illustrates a position sensing mechanism in the form of a curved wire positioned within the vessel lumen.

10 Figure 12A is a cross section of a closure device with a plurality of closure lumens and a static mixer.

Figure 12B is a cross section of a static mixer which is a removable cartridge.

15 Figure 13 is a cross section of a closure device which alternates the precursor exit ports from a first closure compound with the precursor exit ports of a second closure compound.

20 Figure 14A is a cross section of an anti-backflow valve.

Figure 14B is a cross section of an anti-backflow valve.

Figure 15A illustrates a flapper valve disposed within the distal end of a closure device.

25 Figure 15B is a sideview of a flapper valve.

Figure 16 illustrates an embodiment of a closure device that can thermally pretreat tissue prior to the delivery of a closure composition in order to enhance the adhesiveness of tissue to the closure composition.

30 Figure 17 illustrates a cross section of one possible embodiment of a closure device according to the present invention which includes an energy source for pretreating tissue.

35 Figure 18A illustrate a cross section of a

first pressure port.

Figure 18B illustrates a cross section of a second pressure port.

Figures 19A-19D illustrate a method of using the closure device illustrated in Figure 16.

Figure 19A illustrates positioning the plugging catheter within the vessel.

Figure 19B illustrates applying pretreatment energy to the vessel and to tissue adjacent the vessel.

Figure 19C illustrates positioning the closure device so that the position sensor is located outside the vessel.

Figure 19D illustrates delivering the closure composition precursor adjacent the vessel puncture.

Figure 20 illustrates a variation of the embodiment illustrated in Figure 16 in which the sealer/dilator is a cylindrical, tubular element having a lumen within which the plugging catheter can be moved axially (\leftrightarrow).

Figure 21 illustrates a variation of the embodiment illustrated in Figure 16 in which the position of the plugging catheter is fixed relative to the sealer/dilator.

Detailed Description of the Preferred Embodiment

Figures 1A and 1B illustrate a closure device 10 according to the present invention. The closure device 10 may be used to seal a puncture 62 in a vessel 60 such as a femoral artery.

The closure device 10 includes an elongated body 12 with a proximal end 14 and a distal end 16 sized to be inserted into a lumen of a vessel 60. The surface of the elongated body 12 is preferably made of a non-stick material, such as TEFLON, or coated with a biocompatible lubricant. Positioned within the elongated body 12 are one or more closure lumens which extend from

adjacent the proximal end 14 of the device 10 to the distal end 16 of the device 10 for introducing a closure composition precursor 70 adjacent the vessel puncture 62 site. Illustrated in Figures 1A and 1B is a closure device 10 with a first closure lumen 18 with a first precursor entrance port 20 and at least one precursor exit port 22 adjacent the distal end 16. The first precursor entrance port 20 is preferably removably coupleable to a closure composition precursor source 24 for supplying the closure composition precursor 70 to the closure device 10. The first closure lumen 18 may optionally contain an anti-backflow valve 26 to prevent blood from flowing into the first closure lumen 18 from the vessel 60.

The closure composition precursor 70 can be formed of one or more fluent materials that can be flowed from the closure composition precursor source 24 to adjacent the device distal end 16 through the first closure lumen 18. The fluent closure composition precursor 70 is transformed into a non-fluent closure composition *in situ* to effect closure of the puncture 62.

In a preferred embodiment, energy is applied to the closure composition precursor 70 to accelerate its transformation into the non-fluent closure composition. The transformation of the fluent precursor 70 to a non-fluent closure composition may be the result of a phase change (i.e. solidification) of the precursor 70 or a chemical modification of the precursor 70. For example, the precursor 70 may be formed from multiple components which react with each other, optionally accelerated by a catalyst or energy. Alternatively, the precursor 70 may be formed from a single component which reacts with itself, also optionally accelerated by a catalyst or energy.

In embodiments where energy is applied, the

body 12 includes an energy delivery device 28 adjacent the distal end 16. The energy delivery device 28 may be designed to deliver one or more different types of energy including but not limited to electromagnetic radiation (RF, microwave, ultraviolet, visible light, laser), ultrasound, resistive heating, exothermic chemical heating, and frictional heating. The energy source 32 may also function to withdraw energy, i.e., perform cooling. The closure device 10 may also include an energy source attachment mechanism 30 for placing the energy delivery device 28 in energetic communication with an energy source 32.

The body 12 further includes at least one position sensing mechanism 34 adjacent the distal end 16 of the closure device 10 for indicating whether the position sensing mechanism 34 is located within or outside of the vessel 60. The position sensing mechanism 34 should be positioned on the body 12 distal to the precursor exit port 22 so that when the position sensing mechanism 34 is outside the vessel 60 the precursor exit port 22 is also outside the vessel 60. Figure 1A illustrates the closure device 10 with a single position sensing mechanism 34. As illustrated, the closure device 10 may also include a position monitor attachment port 38 for coupling the position sensing mechanism 34 to a position monitor 40. Examples of a position sensing mechanisms 34 include, but are not limited to, a pressure port and an electrical contact switch.

Other sensors (not shown) may also be positioned on the body 12. For instance, a temperature sensor for measuring temperature adjacent the distal end 16 of the body 12 and/or an impedance sensor may be positioned at the distal end 16 of the closure device 10.

The body 12 can include two or more closure lumens for the introduction of closure composition

precursor 70. For example, as illustrated in Figure 2, a second closure lumen 42 may be coupled to a second closure composition precursor source 44 by a second precursor entrance port 46. The second closure lumen 42
5 may also contain an anti-backflow valve 26 to prevent blood flow through the second closure lumen 42.

The closure composition precursor 70 may be introduced adjacent the vessel puncture 62 as a single composition through a first closure lumen 18.
10 Alternately, a first precursor component 113 may be introduced through the first closure lumen 18 and a second precursor component 112 can be introduced through the second closure lumen 42, as illustrated in Figure 2.

The first and second components 113 and 112 can be the
15 same or different and can be introduced simultaneously or at different times. The first and second components 113 and 112 may interact to accelerate the transformation to the non-fluent closure composition at the tissue site 54, for example, by reacting with each other or by one
20 catalyzing the solidification of the other.

Figures 3A-3B illustrate another embodiment of the invention configured to be used with a guidewire 82. As illustrated in Figure 3B, the body 12 can include a guidewire lumen 48 configured to accommodate a guidewire
25 82. The guidewire lumen 48 can include an anti-backflow valve 26. Figure 3C illustrates a cross-section of the device illustrated in Figure 3B.

Figures 4A-4F illustrate a method of using the closure device 10 illustrated in Figures 1A-1B. The
30 closure device 10 is used after a surgical procedure where a vessel 60 such as a femoral artery has been punctured. Angioplasty is a typical surgery which results in puncturing the femoral artery with a catheter.

After the catheter devices from such a surgical
35 procedure have been removed, a sheath 52 typically

remains within a tissue site 54 as illustrated in Figure 4A. The sheath 52 penetrates the skin 56 of the patient and passes through the underlying tissue to a vessel 60.

5 The distal end 16 of the sheath 52 is positioned through a puncture 62 in the vessel 60.

As illustrated in Figure 4B, the closure device 10 is inserted into the sheath lumen 64. The position of the closure device 10 within the sheath 52 may be set by fixing the closure device 10 to the sheath 52. For example, as illustrated, the closure device 10 may include a stop collar 66 which may engage an upper flange 68 on the sheath 52. The distal end 16 of the closure device 10 extends from the sheath 52 such that the position sensing mechanism 34 and precursor exit port 22 are distal relative to the sheath 52 and positioned within the vessel 60.

As illustrated in Figure 4C, the sheath 52 and closure device 10 are simultaneously withdrawn until the position sensing mechanism 34 is sensed to be located outside the vessel 60. Since the precursor exit port 22 is positioned distal relative to the position sensing mechanism, the precursor exit port 22 is necessarily positioned outside the vessel 60 when the position sensing mechanism 34 is outside the vessel 60.

25 As illustrated in Figure 4D, a fluent closure composition precursor 70 is delivered through the first closure lumen 18 and out the precursor exit port 22 after the precursor exit port 22 is determined to be outside the vessel 60. The fluent closure composition precursor 70 should have sufficiently low viscosity to allow the closure composition precursor 70 to flow through the first closure lumen 18. Once delivered, the closure composition precursor 70 accumulates adjacent the vessel 60. The transformation of the closure composition precursor 70 to a non-fluent closure composition serves

to seal the vessel puncture 62. Energy can optionally be delivered from the energy delivery device 28 to the closure composition precursor 70 as illustrated by arrows 72 in order to cause and/or accelerate transformation to the non-fluent closure composition. Alternatively or in addition, a catalyst can be added to catalyze the conversion of the fluent precursor 70 to a non-fluent closure composition.

Figure 4E illustrates the withdrawal of the closure device 10.

In Figure 4F the closure device 10 is completely withdrawn from the tissue site 54 and pressure is being applied at the arrows 74 for a sufficient period of time after the closure composition precursor 70 is delivered to allow the closure composition precursor 70 to transition to non-fluent closure composition.

The body 12 can optionally further include a locking mechanism 76 for coupling the closure device 10 to the sheath 52. For example, as illustrated in Figures 5A and 5B, the locking mechanism 76 can be a threaded nut 78 complementary to threads 80 at the proximal end of the sheath 52. When the closure device 10 is positioned within the sheath 52 the threaded nut 78 is turned to engage the threads 80 on the sheath 52 as illustrated in Figure 5B. As a result, the sheath 52 and closure device 10 move as a unitary body. Movement as a unitary body is desirable to prevent the closure device 10 from moving relative to the sheath 52 when the closure device 10 is withdrawn from the tissue site 54. Other mechanisms can be used to lock the closure device 10 to a sheath 52 including, for example, straps, snap-fit arrangements, bayonet locks, magnets, adhesives, and detents.

Figures 6A-6G illustrate a method of using the closure device 10 illustrated in Figures 3A-3B which include a guidewire 82. As discussed with regard to the

method illustrated by Figures 4A-4F, the method makes use of a sheath 52 left in place after a surgical procedure. Figure 6A illustrates the sheath 52 in place in a tissue site 54 after the surgical procedure..

5 As illustrated in Figure 6B a guidewire 82 is inserted into the vessel 60 through the sheath lumen 64.

Pressure is applied to the skin 56 upstream from the puncture 62 as shown by arrow 76 in Figure 6C to prevent bloodflow through the vessel 60. The sheath 52
10 is then withdrawn from the tissue site 54 along the guidewire 82 as illustrated by arrow 84.

As illustrated in Figure 6D, the guidewire 82 is then thread within the guidewire lumen 48 of the closure device 10 and the distal end is pushed forward
15 through the tissue site 54 until the position sensing mechanism 34 indicates that the position sensing mechanism 34 is within the vessel 60. The distal end 16 of the closure device 10 preferably has the same or larger diameter as the sheath 52 used in the surgical
20 procedure. Since the puncture 62 has been dilated to the diameter of the sheath 52, this sizing reduces leakage of blood between the puncture 62 and the closure device 10.

As illustrated in Figure 6E, the closure device 10 is slowly withdrawn from the vessel 60 until
25 the position sensing mechanism 34 indicates that the position sensing mechanism 34 is located outside the vessel 60. Since the precursor exit port 22 is positioned proximally relative to the position sensing mechanism 34, withdrawal of the position sensing
30 mechanism 34 from the vessel 60 assures that the precursor exit port 22 has been withdrawn from the vessel 60.

As illustrated in Figure 6F, once the precursor exit port 22 is determined to be outside the
35 vessel 60, a closure composition precursor 70 is

delivered through the first closure lumen 18 and out the precursor exit port 22 adjacent the vessel puncture 62.

Figure 6G illustrates the complete withdrawal of the closure device 10 from the tissue site 54.

5 Pressure is applied at the arrows 86 until desired transformation of the fluent closure composition precursor 70 to the non-fluent closure composition is substantially completed.

10 The energy delivery device 28 can be optionally used to deliver a form of energy which functions to accelerate the transformation of the fluent closure composition precursor 70 to non-fluent closure composition. Alternatively or in addition, a catalyst can be added to catalyze the conversion of the fluent
15 precursor 70 to a non-fluent closure composition. Most commonly, energy is used to increase the temperature of the closure composition precursor 70. In one embodiment, the energy delivery device 28 is a microwave antenna positioned on or within the body 12.

20 The guidewire 82 can also include a microwave antenna. When microwave energy is employed, the closure composition precursor 70 preferably includes materials capable of absorbing microwave energy. Examples of such materials include, but are not limited to, hematite (α - Fe_2O_3), maghemite (γ - Fe_2O_3), magnetite (Fe_3O_4), goethite (α - FeOOH), lepidocrocite (γ - FeOOH), ferrihydrite, feroxyhyte (σ - FeOOH), akageneite (β - FeOOH) graphite and
25 amorphous carbon.

The energy delivery device 28 may also be a
30 wave guide 88 for delivery of UV, visible light or laser energy as illustrated in Figure 7A. The closure device 10 includes a waveguide collar 90. Figure 7B illustrates a cross section of the waveguide collar 90. A plurality of waveguides 88 are arranged circumferentially around
35 the collar 90. The light is provided to the waveguides

88 through a cable 92 coupled to a light source 94.

The energy delivery device 28 may also be an electrode for delivering RF energy. The electrode can be a ring electrode encircling the body 12 as illustrated in Figure 1A or a more localized electrode as illustrated in Figure 2. The RF supply wires are run through the body 12 and coupled to the energy source attachment mechanism 30. Alternatively, RF energy may be delivered to the closure composition precursor 70 via the guidewire 82. Other energy sources 32 can also be used, including those that deliver ultrasound, resistive heating, exothermic chemical heating, other forms of electromagnetic radiation, and frictional heating.

Referring again to Figure 1A, one example of a position sensing mechanism 34 is a pressure port coupled to the position monitor attachment port 38 by a first position lumen 97. The position monitor 40 is a pressure sensor coupled to the position monitor attachment port 38 by tubing. As a result, an open channel is created between the pressure port and the pressure sensor allowing the pressure sensor to detect the pressure at the port. The pressure within the vessel 60 is elevated compared with the pressure in the surrounding tissue. As a result, the signal from the pressure sensor indicates whether the position port is located within or outside the vessel 60.

The position sensing mechanism 34 can also be a contact switch 96 as illustrated in Figures 8A and 8B.

The contact switch 96 is coupled to the position monitor attachment port 38 by wires run through the body 12 (not shown). When the contact switch 96 is in contact with the vessel 60 wall the contact switch 96 closes and a circuit (not shown) is completed. However, when the contact switch 96 is not in contact with the vessel 60 wall, the contact switch 96 remains open and the circuit

is not completed. The circuit is monitored to determine the position of the closure device 10 relative to the vessel 60. Alternatively, the circuit can be coupled to the energy delivery device 28 such that the energy cannot
5 be delivered unless the circuit is completed. In one embodiment, the device includes a mechanism which prevents the closure composition precursor 70 from being delivered if the position sensing mechanism 34 is sensed to be within the vessel 60. As a result, energy will not
10 be delivered unless the closure device 10 is properly positioned within the tissue site 54.

In a preferred embodiment, the closure device 10 includes two or more position sensing mechanisms 34 positioned around the closure device 10 where a reading
15 that the sensing mechanisms 34 is outside the vessel 60 occurs when all of the sensing mechanisms 34 are outside of the vessel 60. By having more than one position sensing mechanisms 34 around the closure device 10, false readings from one of the position sensing mechanisms 34
20 are reduced or avoided. For instance, if a single position sensing mechanism 34 is used, the position sensing mechanism 34 may become pressed against the vessel 60 wall resulting in a pressure drop at the position sensing mechanism 34. The position monitor 40
25 would falsely provide a signal indicating that the position sensing mechanism 34 is outside the vessel 60. When a second position sensing mechanism 34 is included, the second position sensing mechanism 34 would still be exposed to the pressure within the vessel 60. As a
30 result, the position monitor 40 would not provide a false signal. Figures 9A and 9B illustrate a closure device 10 with two position sensing mechanisms 34. In Figure 9A, two pressure ports are coupled to a first position lumen 97. In Figure 9B, a first pressure port is coupled to a
35 first position lumen 97 and a second pressure port is

coupled to a second position lumen 101, but both position lumens 97 and 101 are coupled to the same tubing before the tubing is coupled to the pressure sensor.

When the position sensing mechanism 34 is a
5 contact switch 96 or a pressure port, the position sensing mechanism 34 is preferably positioned at least 25 mm from the distal end 16. This positioning assures that the distal end 16 of the closure device 10 remains within the vessel 60 when the closure device 10 is positioned to
10 deliver the closure composition precursor 70. This feature reduces the risk of delivering the closure composition precursor 70 to an improper location on the vessel or within the vessel 60.

Figure 9C illustrates another embodiment of
15 the closure device 10 according to the present invention.

The closure device 10 includes a plurality of pressure ports and a first precursor entrance port 20 and a second precursor entrance port 46. An energy source attachment mechanism 30 is coupled to a plurality of energy delivery
20 devices 28. The closure device 10 includes a guidewire lumen 48 for use with the method described in Figure 6A-6G.

Figures 10A and 10B illustrate another position sensing mechanism 34. A balloon 98 is coupled
25 to the distal end 16 of the closure device 10 by a first and second retaining collar 99. The balloon is positioned over an inflation port 100. The balloon is coupled to an inflation bulb 102 by an inflation lumen 104 and an inflation tube 106.

30 The balloon 98 is deflated when the closure device 10 is positioned within the vessel 60. Once the balloon 98 enters the vessel 60, the balloon 98 is inflated to a diameter greater than the diameter of the sheath 52 and thus the puncture 62. The closure device
35 10 is then withdrawn until the resistance of the balloon

98 against the puncture 62 is felt as illustrated in Figure 10B. The resistance indicates that the precursor exit port 22 is outside the vessel 60 and properly positioned for application of the closure composition precursor 70.

Figure 11 illustrates yet another embodiment of a position sensing mechanism 34. According to this embodiment, a curved wire 89 is positioned within the vessel 60. As the closure device 10 is withdrawn, resistance is felt when the curved wire 89 is pushed up against the interior of the vessel lumen. The closure precomposition exit ports 22 are positioned such that when the resistance is felt, the precomposition ports are known to be positioned outside of the vessel 60.

Each position sensing mechanism 34 can be distally positioned 0.5-30 mm from the precursor exit port 22 and more preferably 3.0-9.0 mm from the precursor exit port 22. These distances allow the closure composition precursor 70 to be reliably delivered outside the vessel 60 once the closure device 10 is positioned for delivery of the closure composition precursor 70.

A variety of additional sensors may be used in combination with the present invention. For example, temperature sensors may be positioned adjacent the distal end 16 of the closure device 10 for detecting the temperature adjacent the distal end 16. The temperature sensors may be a thermocouple positioned on the surface of the body 12 (not shown) and hardwired to electrical contacts within a sensor monitor attachment port (not shown). These sensors are useful for regulating the amount of energy being delivered to the vessel 60 and tissue site 54 adjacent the closure device 10 and for preventing tissue damage and ablation due to excess heat application.

Impedance sensors may also be employed when RF

is used in order to monitor the amount of energy being delivered to the tissue site 54.

When the closure composition precursor 70 is formed of two or more components, the closure device 10 can optionally include a static mixer 108 for mixing different closure composition precursor components before the closure composition precursor 70 exits the precursor exit port or ports 22. Figure 12A illustrates a static mixer 108 incorporated into the closure device 10. The first closure lumen 18 and the second closure lumen 42 intersect at least one time before terminating in at least one precursor exit port 22. The static mixer 108 can also be a cartridge 110 incorporated into the body 12 of the closure device 10 as illustrated in Figure 12B. The intersection of the first and second lumens 18 and 42 assures that the first precursor component 113 and second precursor component 112 are mixed before reaching the at least one precursor exit port 22.

The configuration of precursor exit ports 22 can also serve to assure adequate mixing of the first precursor component 113 and second precursor component 112. As illustrated in Figure 13, the precursor exit ports 22 corresponding to the first precursor component 113 alternate with the precursor exit ports 22 corresponding with the second precursor component 112. As a result, the first and second precursor components 112 and 113 are mixed outside the closure device 10.

An anti-backflow valve 26 which is suitable for use in a closure lumen 18 or 42 illustrated in Figures 14A and 14B. The valve 26 has a composition entrance 114 and a composition exit 116. Figure 14A illustrates that when a fluid flows from the entrance 114 to the exit 116, a diaphragm 118 slides forward to allow the closure composition precursor 70 to flow freely through the valve 26. Figure 14B illustrates that when a

fluid flows from the exit 116 to the entrance 114, the fluid places pressure against the backside of the diaphragm 118 causing the diaphragm 118 to slide against the entrance 114 sealing the entrance 114 and preventing
5 a flow of fluid through the valve 26.

An example of a suitable anti-backflow valve 26 for use in the guidewire lumen 48 adjacent the distal end 16 of the device 10 is a flapper valve 120 as illustrated in Figures 15A and 15B. Examples of anti-
10 backflow valves 26 for the guidewire lumen 48 which may be positioned adjacent the proximal end 14 of the device 10 include, but are not limited to, duckbill valves, hemostasis valves, and Tuhoy-Bourse valves. The flapper valve 120 is preferably formed of an elastomeric material
15 such as medical grade silicone rubber. The configuration, as illustrated by Figure 15B, may be a cylindrical section 126 transitioning into a conical portion 128. The conical portion 128 has a series of slits 122 which allow various implements to pass through
20 the valve 26. The thickness of the flaps 124 and the flexibility of the elastomeric material will be balanced to provide memory sufficient to close the puncture 62 as the implements are withdrawn and provide a fluid seal. Blood pressure against the outer surface of the conical
25 portion 128 will cause the flapper valve 120 to close more tightly.

The body 12 is formed of any suitable, relatively flexible material. Suitable materials include, but are not limited to, polyethylene, PEBAX,
30 polytetrafluoroethylene (TEFLON) and polyurethane.

A variety of different closure composition precursors 70 and non-fluent closure compositions can be used in the present invention. The fluent closure composition precursor 70 and non-fluent closure
35 composition should be biocompatible and preferably

bioresorbable. The closure composition should be also capable of forming a strong puncture seal and be able to seal larger sized vessel punctures 62, e.g., punctures 62 formed by 8 french or larger needles.

5 Examples of closure compositions that can be
used with the device 10 and method of the present
include, but are not limited to sealants and adhesives
produced by Protein Polymer Technology; FOCALSEAL
produced by Focal; BERIPLAST produced by Centeon (JV
10 Behringwerke & Armour); VIVOSTAT produced by ConvaTec
(Bristol-Meyers-Squibb); SEALAGEN produced by Baxter;
FIBRX produced by CyoLife; TISSEEL AND TISSUCOL produced
by Immuno AG; QUIXIL produced by Omrix Biopharm; a PEG-
collagen conjugate produced by Cohesion (Collagen);
15 HYSTOACRYL BLUE produced by Davis & Geck; NEXACRYL,
NEXABOND, NEXABOND S/C, and TRAUMASEAL produced by
Closure Medical (TriPoint Medical); OCTYL CNA produced by
Dermabond (Ethicon); TISSUEGLU produced by Medi-West
Pharma; and VETBOND produced by 3M. Examples of two part
20 closure compositions which may be used are listed in
Table 1.

TABLE 1

CLASS OF ADHESIVE	PART A	PART B
(Meth) Acrylic (redox initiated)	(Meth)acrylic functional monomers and oligomers with oxidant initiator	(Meth)acrylic functional monomers and oligomers with reductant initiator
Polyurethane	Poly isocyanate	Hydrocarbon polyol, polyether polyol, polyester polyol
Polyurea	Poly isocyanate	Hydrocarbon polyamine, polyether polyamine
lonomer	Polyvalent metal cation	Acrylic acid (co) polymer, alginate
Epoxy	Epoxy resin	Aliphatic polyamine, catalyst
Protein/dialdehyde	Gelatin	Glutaraldehyde

Another aspect of the present invention relates to a method for improving the adhesiveness of a surface of living tissue by treating the tissue surface with a form of energy which thermally modifies the tissue surface and renders the surface more readily bonded or adherent to tissue adhesives, sealants, glues and the like. The thermal modification preferably includes blanching the tissue surface. The thermal modification is believed to reduce the water content at the tissue surface, remove materials at the tissue surface which interfere with the adhesiveness of tissue surfaces to sealants and adhesives, change the topography at the tissue surface, and preferably increase the surface area at the tissue surface, all of which serve to increase the tissue surface's ability to adhere sealants and adhesives.

In one embodiment, the method includes exposing a tissue surface to be so treated, which optionally includes the action of forming new tissue surfaces such as by cutting tissue with a scalpel or tool, or by introducing a medical instrument into previously continuous tissue such as with a cannula, introducer, catheter, or trocar, to provide new tissue surface(s) surrounding the instrument. For example, this step is encompassed by the step of introducing a closure device of the present invention into tissue.

After a tissue surface to be treated has been exposed, the tissue surface is contacted with a source of energy that functions to heat the surface of the tissue. Examples of suitable forms of energy include but are not limited to electromagnetic energy (RF energy, light, and microwave energy), ultrasound, and other thermal heat sources. In one particular embodiment, RF energy may be delivered to the tissue surface from a metallic electrode (monopolar) of any convenient shape, such as ring or needle. In another particular embodiment, RF energy is delivered through a saline solution provided by a microporous membrane (MPM). In yet another particular embodiment, the RF energy has an intermittent and variable waveform, such as so-called "coagulation" waveforms, which can serve to increase the bondability of the tissue surface.

Energy is applied until a degree of "blanching" has been achieved and the ability to bond to the tissue surface is increased. It is believed that the energy thermally modifies the tissue surface and causes the tissue to be more adherent to sealants and adhesives, such as closure composition used in the present invention.

While the pretreatment method is being described herein with regard to its use in combination

with a closure device of the present invention, it is envisioned that the pretreatment method is a tissue priming method which may be used to enhance the adhesiveness of any tissue surface to which a tissue glue
5 or sealant is to be applied and thus may be used with other methods for joining tissues other than those described in this application. It is believed that this method can be beneficially used in a variety of protocols or procedures that use non-mechanical agents such as
10 glues, adhesives and sealants to join tissue. It is also believed that this method can be beneficially used in protocols or procedures that use mechanical mechanisms, such as mechanical fasteners, to join tissue. Further, it is believed that the pretreatment method will be
15 beneficial for improving bonding strength to and between tissue surfaces in procedures relying on chemical adhesion, including covalent bonding, as well as mechanical interlocking.

Figure 16 illustrates an embodiment of a
20 closure device 140 that includes an energy source 162 for pretreating tissue prior to the delivery of a closure composition in order to enhance the adhesiveness of tissue to the closure composition. The closure device 140 may be used to seal a puncture 181 in a vessel 166
25 such as a femoral artery. The closure device 140 includes a sealer/dilator 142 with a proximal end 144 and a distal end 146 that serves as a sealer and tissue dilator. The surface of the sealer/dilator 142 is preferably made of a non-stick material, such as TEFLON,
30 or coated with a biocompatible lubricant. Positioned within the sealer/dilator 142 are one or more closure lumens that extend from adjacent the proximal end 144 of the device to the distal end 146 of the device for introducing a closure composition precursor adjacent the
35 vessel puncture site.

Illustrated in Figure 16 is a closure device 140 with a single closure lumen 148 with a precursor entrance port 150 and at least one precursor exit port 152 adjacent the distal end 146. The precursor entrance port 150 is preferably removably coupleable to a closure composition precursor source 154 for supplying the closure composition precursor 183 to the closure device 140. The closure lumen 148 may optionally contain an anti-backflow valve 156 to prevent blood from flowing into the closure lumen 148 from the vessel 166.

The closure composition precursor 183 can be formed of one or more fluent materials that can be flowed from the closure composition precursor source 154 to adjacent the device distal end 146 through the closure lumen 148, such as the closure composition precursors described in this application. The fluent closure composition precursor is transformed into a non-fluent closure composition *in situ* to effect closure of the puncture 181.

The sealer/dilator 142 includes an energy delivery device 158 adjacent the distal end 146 for pretreating the tissue site 184 prior to delivering the closure composition precursor 183 to the tissue site 184.

The energy delivery device 158 may be designed to deliver one or more different types of energy including but not limited to electromagnetic radiation (RF, microwave, ultraviolet, visible light, laser), ultrasound, resistive heating, exothermic chemical heating, and frictional heating. The closure device 140 also includes an energy source attachment mechanism 160 for placing the energy delivery device 158 in energetic communication with an energy source 162.

A plugging catheter 163 sized to fit within a vessel lumen extends from the distal end 146 of the sealer/dilator 142. In one embodiment, the

sealer/dilator 142 is actually a cylindrical, tubular element having a lumen within which the plugging catheter 163 can be moved axially. The plugging catheter 163 includes at least one position sensing mechanism 164 for
5 indicating whether the position sensing mechanism 164 is located within or outside of the vessel 166. The position sensing mechanism 164 should be positioned on the plugging catheter 163 distal to the precursor exit port 152 so that when the position sensing mechanism 164
10 is outside the vessel 166 the precursor exit port 152 is also outside the vessel 166.

Figure 16 illustrates the closure device 140 with dual position sensing mechanisms 164. As illustrated, the closure device 140 may also include a
15 position monitor attachment port 168 for coupling the position sensing mechanism 164 to a position monitor 170. Examples of a position sensing mechanisms 164 include, but are not limited to, a pressure port and an electrical contact switch.

20 The sealer/dilator 142 and plugging catheter 163 also include a guidewire lumen 169 configured to accommodate a guidewire 179. The guidewire lumen 169 can include an anti-backflow valve or hemostasis valve.

Other sensors (not shown) may also be
25 positioned on the plugging catheter 163 or the sealer/dilator 142. For instance, a temperature sensor for measuring temperature adjacent the distal end 146 of the sealer/dilator 142 and/or an impedance sensor may be positioned at the distal end 146 of the sealer/dilator
30 142.

The sealer/dilator 142 can include two or more closure lumens for the introduction of closure composition precursor 183. For example, a second closure lumen may be coupled to a second closure composition
35 precursor source by a second precursor entrance port (not

shown). The second closure lumen may also contain an anti-backflow valve to prevent blood flow through the second closure lumen.

5 The closure composition precursor 183 may be introduced adjacent the vessel puncture 181 as a single composition through a single closure lumen 148. Alternately, a first composition may be introduced through the closure lumen 148 and a second composition can be introduced through the second closure lumen. The
10 first and second compositions can be the same or different and can be introduced simultaneously or at different times. The first and second compositions may interact to accelerate the transformation to the non-fluent closure composition at the tissue site 184, for
15 example, by reacting with each other or by one catalyzing the solidification of the other.

In a preferred embodiment, the closure device 140 also includes an energy source 162 for applying energy 167 to the closure composition precursor 183 to
20 accelerate its transformation into the non-fluent closure composition. The transformation of the fluent closure composition 183 precursor to a non-fluent closure composition may be the result of a phase change (i.e. solidification) of the precursor 183 or a chemical
25 modification of the precursor 183. For example, the precursor 183 may be formed from multiple components which react with each other, optionally accelerated by a catalyst or energy 167. Alternatively, the precursor 183 may be formed from a single component that reacts with
30 itself, also optionally accelerated by a catalyst or energy 167.

In embodiments where energy 167 is applied, the energy delivery device 158 on the elongated body or an additional energy delivery device 158 is used to
35 deliver one or more different types of energy 167

including but not limited to electromagnetic radiation (RF, microwave, ultraviolet, visible light, laser), ultrasound, resistive heating, exothermic chemical heating, and frictional heating which serves to
5 accelerate the conversion of the closure composition precursor 183 to a non-fluent closure composition.

Figures 16-17 illustrate one possible embodiment of a closure device 140 according to the present invention that includes an energy source 162 for
10 pretreating tissue. As illustrated, the closure device 140 includes a sealer/dilator 142 with a proximal end 144 and a distal end 146 which serves as a sealer and tissue dilator. The surface of the sealer/dilator 142 is preferably made of a non-stick material, such as TEFLON,
15 or coated with a biocompatible lubricant. Positioned within the sealer/dilator 142 is a central lumen 145. The central lumen 145 serves as a lumen for a guidewire 179 and plugging catheter 163. The central lumen 145 also serves as a lumen for delivery of the closure
20 composition precursor 183. As illustrated, the central lumen 145 is also connected to a precursor entrance port 150 adjacent the proximal end 144 of the closure device 140 and extends to a precursor exit port 152 adjacent the distal end 146. The precursor entrance port 150 is
25 preferably removably coupleable to a closure composition precursor source 154 (not shown) for supplying the closure composition precursor 183 to the closure device 140. Tubing 147, such as TYGON tubing, with a valve 149 may be attached to the precursor entrance port 150 for
30 facilitating attachment of a closure composition precursor source 154 (not shown).

The sealer/dilator 142 includes an energy delivery device 158 adjacent the distal end 146 for pretreating the tissue site 154 prior to delivering the
35 closure composition precursor 183 to the tissue site 154.

The energy delivery device 158 is energetically connected via a conductive metal tube 155 and a wire 151 to an energy source attachment mechanism 160 for placing the energy delivery device 158 in energetic communication
5 with an energy source 162 (not shown).

The sealer/dilator 142 also includes threading 177 adjacent its proximal end 144 for attaching a hemostasis/lock valve 176 to the sealer/dilator distal end 146.

10 A plugging catheter 163 sized to fit within a vessel lumen extends through the central lumen 145 and out the distal end 146 of the sealer/dilator 142. The proximal end of the plugging catheter 163 includes a guidewire Luer 157 for positioning a guidewire 179 within
15 a guidewire lumen 169. The plugging catheter 163 can optionally include a locating mark 178 which can be used to indicate how far the plugging catheter 163 is extending from the distal end 146 of the sealer/dilator 142.

20 The plugging catheter 163 includes first and second position sensing mechanisms 164A, 164B for indicating whether the first and second position sensing mechanisms 164A, 164B are located within or outside of the vessel 166. As can be seen, the first position
25 sensing mechanism 164A is distal relative to the second position sensing mechanism 164B. This enables the plugging catheter 163 to be positioned such that the first position sensing mechanism 164A is inside the vessel 166 and the second position sensing mechanism 164B
30 is outside the vessel 166.

One example of a position sensing mechanism 164 is a pressure port coupled to the position monitor attachment port 168 by a position lumen. Figures 18A and 18B illustrate a cross section of the plugging catheter
35 163 which includes a first position sensing mechanism

164A and a second position sensing mechanism 164B. As illustrated in Figure 18A, the first position sensing mechanism 164A includes a first position sensor lumen 163A and a pair of first pressure ports 165A. Also
5 illustrated in Figure 18A is the second position sensor lumen 163B of the second position sensing mechanism 164B. Figure 18B illustrates a pair of second pressure ports 165B of the second position sensing mechanism 164B.

As illustrated in Figure 17, the closure
10 device 140 also includes marker port capillary tubes 171 A, 171 B attached to the first and second position sensor lumens 163A and 163B respectively.

As can be seen from Figures 18A and 18B, the first and second pressure ports 165A, 165B are preferably
15 angularly offset relative to each other so that the pressure ports 165A and 165B will not be blocked by a same obstruction. Similarly, at least a pair of pressure ports is preferably used in each position sensing mechanism 164 so that a given position sensing mechanism
20 164 is not blocked by a single obstruction. These design features enhance the reliability of the position sensing mechanisms 164.

Also illustrated in Figures 18A and 18B is a guidewire lumen 169 configured to accommodate a guidewire
25 179 running through the plugging catheter 163. The guidewire lumen 169 can include an anti-backflow valve 156 or hemostasis valve 176.

Other sensors may also be positioned on the plugging catheter 163. For instance, as illustrated in
30 Figure 17, a temperature sensor 159 for measuring temperature adjacent the distal end 146 of the sealer/dilator 142 may be positioned at the distal end 146 of the sealer/dilator 142. As also illustrated, the temperature sensor 159 is connected to a temperature
35 sensor wire 173 which can be attached to a temperature

sensor connector 175.

Figures 19A-19D illustrate a method of using the closure device 140 illustrated in Figure 16. As illustrated in Figure 19A, the guidewire 179 is thread
5 within the guidewire lumen 169 of the closure device 140 and the plugging catheter 163 is pushed forward through the tissue site 184 until the position sensor 174 indicates that the position sensor 174 is within the vessel 166. The plugging catheter 163 of the closure
10 device 140 preferably has the same or larger diameter as the sheath used in the surgical procedure. Since the puncture 181 has been dilated to the diameter of the sheath, this sizing reduces leakage of blood between the puncture 181 and the closure device 140.

15 As illustrated in Figure 19B, the closure device 140 is pushed into the tissue site 184 until the distal end 146 of the sealer/dilator 142 is adjacent the vessel 166. Because the distal end 146 of the sealer/dilator 142 is significantly larger than the
20 puncture 181 in the vessel 166, resistance will be felt when the distal end 146 of the sealer/dilator 142 is pushed against the vessel 166. Energy 167 is then applied by the energy delivery device 158 to pretreat the vessel 166 and tissue adjacent the vessel 166.

25 As illustrated in Figure 19C, the closure device 140 is then slowly withdrawn from the vessel 166 until the position sensor 174 indicates that the position sensor 174 is located outside the vessel 166. Since the precursor exit port 152 is positioned proximally relative
30 to the position sensing mechanism 164, withdrawal of the position sensing mechanism 164 from the vessel 166 assures that the precursor exit port 152 has been withdrawn from the vessel 166.

35 As illustrated in Figure 19D, once the precursor exit port 152 is determined to be outside the

vessel 166, a closure composition precursor 183 is delivered through the closure lumen 148 and out the precursor exit port 152 adjacent the vessel puncture 181.

5 Figure 20 illustrates a variation of the embodiment illustrated in Figure 16 in which the sealer/dilator 142 is a cylindrical, tubular element having a lumen within which the plugging catheter 163 can be moved axially (\leftrightarrow). In this variation, the plugging catheter 163 may include a retraction locking mechanism
10 190 that limits how far the plugging catheter 163 may be withdrawn from the body of the patient through the sealer/dilator 142. As illustrated, the retraction locking mechanism 190 may be a member extending from the surface of the plugging catheter 163 that prevents the
15 plugging catheter 163 from being withdrawn further.

Figure 21 illustrates a variation of the embodiment illustrated in Figure 16 in which the position of the plugging catheter 163 is fixed relative to the sealer/dilator 142. As illustrated, the closure device
20 140 includes dual position sensing mechanisms 164A, 164B and dual capillaries 171A and 171 B. Preferably, a closure composition precursor 183 is delivered adjacent to the vessel 166 when position sensing mechanism 164A is detected to be within the vessel 166 and position sensing
25 mechanism 164B is detected to be outside the vessel 166.

The embodiment illustrated further includes a third position sensing mechanism 164C and capillary 171 C which is used as a safety device to detect when the sealer/dilator 142 is within the vessel 166.

30 Another aspect of the present invention relates to a method for improving the adhesiveness of a surface of living tissue by treating the tissue surface with a chemical agent which modifies the tissue surface and renders the surface more readily bonded or adherent
35 to tissue adhesives, sealants, glues and the like. The

chemical modification may optionally include a degree of surface denaturization, a reduction in the water content at the tissue surface, removal of materials at the tissue surface which interfere with the adhesiveness of tissue surfaces to sealants and adhesives, a change the topography at the tissue surface, and preferably an increase in the surface area at the tissue surface, all of which serve to increase the tissue surface's ability to adhere sealants and adhesives.

10 In one embodiment, the method includes exposing a tissue surface to be so treated, which optionally includes the action of forming new tissue surfaces such as by cutting tissue with a scalpel or tool, or by introducing a medical instrument into
15 previously continuous tissue such as with a cannula, introducer, catheter, or trocar, to provide new tissue surface(s) surrounding the instrument. For example, this step is encompassed by the step of introducing a closure device of the present invention into tissue.

20 After a tissue surface to be treated has been exposed, the tissue surface is contacted with a suitable chemical agent. In one variation, a basic chemical agent (i.e., having a pH greater than 7) capable of modifying a tissue surface is used. Examples of suitable basic
25 chemical agents include but are not limited to aqueous sodium bicarbonate, aqueous sodium carbonate, water solutions or suspensions of alkali or alkali earth oxides and hydroxides, aqueous ammonia, water soluble amines such as alkanol amines, basic amino acids such as lysine
30 and poly(lysine), aqueous sodium lysinate, and basic proteins such as albumin. In another variation, an acidic chemical agent (i.e., having a pH less than 7) having an osmolality above that of blood is used which is capable of modifying a tissue surface. In yet another
35 variation, a chemical agent which can serve as a tissue

etchant is used. Examples of suitable tissue etchants include, but are not limited to salicylic acid, carboxylic acids, α -hydroxy carboxylic acids, and peroxides.

5 While the chemical pretreatment method is being described herein with regard to its use in combination with a closure device of the present invention, it is envisioned that the chemical pretreatment method is a tissue priming method which may
10 be used to enhance the adhesiveness of any tissue surface to which a tissue glue or sealant is to be applied and thus may be used with other methods for joining tissues other than those described in this application. It is believed that this method can be beneficially used in a
15 variety of protocols or procedures that use non-mechanical agents such as glues, adhesives and sealants to join tissue. It is also believed that this method can be beneficially used in protocols or procedures that use mechanical mechanisms, such as mechanical fasteners, to
20 join tissue. Further, it is believed that the pretreatment method will be beneficial for improving bonding strength to and between tissue surfaces in procedures relying on chemical adhesion, including covalent bonding, as well as mechanical interlocking.

25 **EXAMPLE**

1. Procedure For Pretreating Tissue

 The following example provides an exemplary procedure for pretreating tissue with energy in order to enhance the adhesiveness of the pretreated tissue to an
30 adhesive material.

 Tissue samples were prepared by cuffing beef flank steak into specimens about 35 mm long by 8 mm wide by 2 mm thick with a scalpel. Care was taken to ensure that the muscle fibrils were aligned lengthwise and the
35 connective tissue between fibrils was intact. A set of

12 specimens was soaked in physiologic saline (NaCl; equal to about 0.9% wt.) for 30 minutes just prior to use. The saline soaked tissue was used as a model for living tissue, which would contain intercellular fluid and blood encountered during any tissue sealing or wound closure medical procedure.

An electrode comprised of a metal cap 6 mm in diameter and 2 mm deep on the end of a plastic wand was fitted with a thermocouple for measuring the temperature at the electrode surface. The electrode was connected to an Apical, Inc. (Menlo Park, CA) Radio Frequency (RF) generator.

Some of the tissue samples were treated with RF energy immediately prior to bonding with a tissue adhesive by the following method:

a) an aluminum pan containing a porous towel saturated with a physiologic saline solution was electrically connected to the RF generator via a standard electrosurgical grounding pad;

b) a tissue sample to be treated was laid onto the moist towel and the electrode wand touched endwise to one end of the tissue sample such that a circular area approximately 6 mm in diameter was in contact with the electrode and could be treated;

c) RF energy at a power of 10 watts in the frequency range of 300-700 kHz was applied to the electrode and to the tissue surface;

d) the electrode temperature was monitored during the application of energy and increased about 1-2°C/second in the temperature range of 25-65°C;

e) the electrode treatment temperature was maintained at the desired level by the Apical RF Generator until treatment was manually stopped after the desired time at temperature; and

f) the twelve energy treated tissue samples

were set up in pairs to form six lap shear specimens.

5 The energy treated tissue samples were then
evaluated for the shear strength of the resultant lap
bond. A standard gelatin/aldehyde two part tissue
adhesive was spread onto the treated portion of one
energy treated tissue sample and then compressed against
a second energy treated tissue sample to form a lap shear
specimen assembly. Bond area was calculated as the
product of the bond width and the overlap of the tissue
10 surfaces.

Lap shear bond strength evaluation was done on
the six replicate specimen assemblies prepared for each
set of control and RF treatment conditions. Bond
strength was measured using a Chatillion Stress-Strain
15 instrument. Bond strengths were taken as the average of
the six replicates.

Experimental results from this experiment are
tabulated in Table 2. As can be seen from the data
presented in the table, pre-treatment of tissue with RF
20 energy to a temperature of 50°C for 5 seconds increased
the average lap shear bond strength by 34% and increased
the greatest observed strength in the sample population
by 66%. These results demonstrate the efficacy of the
pre-treatment method for increasing the bond strength of
25 energy treated tissue relative to non-energy pretreated
tissue.

While the present invention is disclosed by
reference to the preferred embodiments and examples
detailed above, it is to be understood that these
30 examples are intended in an illustrative rather than
limiting sense, as it is contemplated that modifications
will readily occur to those skilled in the art, which
modifications will be within the spirit of the invention
and the scope of the appended claims.

TABLE 2

Sample	Bond Width, mm	Bond Overlap, mm	Bond Failure, X 100 lb	Lap Shear Bond Strength, g/cm ²	AVG	STD DEV
Control						
No Treatment	9	10	58	23		
Saline Soak	14	8	42	10		
	10	10	42	11		
	9	10	44	22		
	11	10	48	18		
					215	47
50 C / 5 sec Pre-Treatment Saline Soak						
	9	10	41	27		
	8	8	42	28		
	7	8	60	46		
	8	10	35	19		
	7	11	68	41		
	6	10	20	11		
					290	131